

**Purpose:** To compare the efficacy of prophylactic antibiotics in reduction of post-operative infections in patients undergoing ureterorenoscopy (URS) as the intervention.

**Materials and Methods:** The study is a open-labeled, prospective, randomized controlled trial. Between 2012 to 2015, 45 patients with preoperative sterile urine undergoing URS were randomly and equally allocated by the randomization to three groups, and each group received prophylactic antibiotics with single-dose intravenous cefazolin (1gm), oral cefuroxime (500mg) or placebo (control group), respectively. The Urine analysis and urine cultures were obtained around postoperative day 5 to 7. We defined pyuria as WBC  $\geq 10$ /HPF at urine sediment study, and significant bacteriuria was defined as  $\geq 105$  CFU pathogens/ml in the urine. Febrile urinary tract infection (fUTI) was defined as body temperature more than 38 Celsius degree with pyuria or significant bacteriuria within 7 days post-operatively.

**Results:** Total 45 patients were recruited for the analysis. The post-operative pyuria were significantly lower in patients with prophylaxis than the placebo group (42.2% vs. 70.0%,  $p = 0.04$ ). Patients receiving prophylactic antibiotics with cefazolin and oral cefuroxime were subjected to significantly lower risks of pyuria compared with the control group (36.0% and 48.5% vs. 70%,  $p < 0.05$ ).

There are the trends that the rates of bacteriuria and fUTI were be lower in patients underwent prophylaxis, though they were not statistically significant (3.5% vs 9.8%,  $p = 0.1$ , 1.1% vs. 4.9%,  $p = 0.08$ ). There was no significant difference in rates of bacteriuria and fUTI between the three groups.

**Conclusions:** Antibiotic prophylaxis significantly reduces the incidence of pyuria following URS and tends to decreased the risk of bacteriuria and UTI.

#### IPD23:

#### PSYCHOGENIC CAUSE IS NOT THE MAIN RISK FACTOR FOR ERECTILE DYSFUNCTION IN YOUNG MEN COMPARED TO THE AGING GROUP

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**Purpose:** The erectile dysfunction (ED) is more prevalent in elderly, and the common risk factors for patients above the age of 40 have been well studied. However, there is increasing tendency of men under the age of 40 seeking for help for ED. Conventionally, psychological factor is considered to be the likeliest reason in these patients. The aim of this study is to compare the prevalence of psychogenic cause and the other risk factors associated with ED between the young and aging groups.

**Materials and Methods:** From June 2013 to November 2014, total 331 patients presented to our out-patient clinic with chief complaint of ED were enrolled. The clinical characteristics, underlying diseases, current medications, IIEF-5 questionnaire, Hospital Anxiety and Depression Scale (HADS), biochemical and hormonal profiles and penile duplex Doppler ultrasonography were collected. The patients were divided into young age group (age  $\leq 40$ ) and old age group (age  $> 40$ ). Chi-square test and Fisher's exact test were used to evaluate the difference in the prevalence of the risk factors between the two groups.

**Results:** Of the 331 patients, 60 (18.1%) were in the young age group. According to the score of IIEF-5, patients in the young age group were though to have mild to moderate disease (IIEF-5: 12–21), compared to the patient in the old age group who were more likely to have moderate to severe disease (IIEF-5: 5–11) ( $P = 0.015$ ). The anxiety portion of the HADS showed no difference between two groups; however, higher prevalence of depression was noted in the old age group ( $P = 0.024$ ). In addition, higher prevalence of hypertension as well as diabetes mellitus was found in the old age group. No difference in the over-weight or obesity parameter (BMI), dyslipidemia parameters and the smoking condition were found between the two groups. The old age group also had a higher frequency on the findings of penile duplex Doppler, such as arterial insufficiency or veno-occlusive dysfunction ( $P < 0.001$ ).

**Conclusion:** The prevalence of anxiety or depression in the young men with ED is not higher than those in old age group. Instead, the elderly with ED tend to have depression problem. Similar prevalence of dyslipidemia

and BMI distribution in the two groups suggest that young men with ED indeed possess some organic risk factors.

#### IPD15:

#### CHANGING TRENDS IN THE AETIOLOGY AND MANAGEMENT OF MALE URETHRAL STRICTURE DISEASE: A SURVEY FROM 13 CENTRES IN CHINA

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**Purpose:** To determine whether there were any changes in the aetiology and management of urethral strictures in China.

**Materials and Methods:** The data from 4764 male patients with urethral stricture disease who underwent treatment at 13 medical centres in China between 2005 and 2010 were retrospectively collected. The databases were analysed for the possible causes, site and treatment techniques for the urethral stricture, as well as for changes in the urethral stricture aetiology and management.

**Results:** The most common cause of urethral strictures was trauma, which occurred in 2466 patients (51.76%). The second most common cause was iatrogenic injuries, which occurred in 1643 patients (34.49%). The most common techniques to treat urethral strictures were endourological surgery (1740, 36.52%), anastomotic urethroplasty (1498, 31.44%) and substitution urethroplasty (1039, 21.81%). A comparison between the first three years and the last three years showed that the constituent ratio of endourological surgery decreased from 54% to 32.75%, whereas the constituent ratios of anastomotic urethroplasty and substitution urethroplasty increased from 26.73% and 19.18% to 39.93% and 27.32%, respectively ( $P < 0.05$ ).

**Conclusions:** During recent years, there has been an increase in the incidence of urethral strictures caused by trauma and iatrogenic injury. Endourological urethral surgery rates decreased significantly, and open urethroplasty rates increased significantly during the latter three years analysed.

#### ISTUA Podium-4

##### Basic

#### IPD24:

#### NOVEL CANCER THERAPEUTICS WITH ALLOSTERIC MODULATION OF THE MITOCHONDRIAL C-RAF/DAPK COMPLEX BY RAF INHIBITOR COMBINATION THERAPY

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**Purpose:** Mitochondria are the powerhouses of cells. Mitochondrial C-Raf is a potential cancer therapeutic target, as it regulates mitochondrial function and is localized to the mitochondria by its N-terminal domain. However, Raf inhibitor monotherapy induced S338 phosphorylation of C-Raf (pC-Raf<sup>S338</sup>) and impede therapy which is urged to be overcome in clinical practice.

**Materials and Methods:** We analyzed the growth-inhibition effect of Sorafenib and GW5074 combination therapy on multiple normal and cancer cell lines by MTT assay *in vitro* and its anticancer effect with xenograft and orthotopic metastasis animal models *in vivo*. The molecular mechanisms involved in the regulation of mitochondrial function have been investigated by means of western blotting analysis, fractionation, immunoprecipitation assays and FACS analysis. The protein expression in cancer tissues and normal counterparts was examined by immunohistochemistry assay.

**Results:** This study identified the interaction of C-Raf with S308 phosphorylated DAPK (pDAPK<sup>S308</sup>), which together became co-localized in the mitochondria to facilitate mitochondrial remodelling. Combined use of the Raf inhibitors sorafenib and GW5074 had synergistic anti-cancer effects *in vitro* and *in vivo*, but targeted mitochondrial function, rather than the canonical Raf signaling pathway. C-Raf depletion in knock-out MEF<sup>C-Raf/-</sup> or siRNA knock-down ACHN renal cancer cells abrogated the cytotoxicity of combination therapy. Crystal structure simulation showed that GW5074 bound to C-Raf and induced a C-Raf conformational change that enhanced sorafenib binding affinity. In the presence of pDAPK<sup>S308</sup>, this drug-target interaction compromised the mitochondrial targeting effect of the N-terminal domain of C-Raf, which induced two-hit damages to cancer cells. First, combination therapy facilitated pC-Raf<sup>S338</sup> and pDAPK<sup>S308</sup> translocation from mitochondria to cytoplasm, leading to mitochondrial dysfunction and ROS generation. Second, ROS facilitated PP2A-mediated de-phosphorylation of pDAPK<sup>S308</sup> to DAPK. PP2A then dissociated from the C-Raf-DAPK complex and induced profound cancer cell death. Increased pDAPK<sup>S308</sup> modification was also observed in renal cancer tissues, which correlated with poor disease-free survival and poor overall survival in renal cancer patients.

**Conclusions:** Besides mediating the anti-cancer effect, pDAPK<sup>S308</sup> may serve as a predictive biomarker for Raf inhibitors combination therapy, suggesting an ideal pre-clinical model that is worthy of clinical translation.

#### IPD25:

#### HIGHER EXPRESSION OF ACETYL-TUBULIN MAY INDUCE DOCETAXEL RESISTANCE IN PROSTATE CANCER CELLS

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**Purpose:** Docetaxel-based chemotherapy has generally been considered as one of the effective treatments for prostate cancer. Unfortunately, clinical treatment with docetaxel often encounters a number of undesirable side effects, including drug resistance. Therefore, it has become essential to identify molecular events that may be associated with the development of docetaxel resistance. Tubulin isoforms have been previously examined for their resistant ability to docetaxel in many cancers, but their real mechanisms remained unclear. In this study, we evaluated the feasibility of employing docetaxel as a cytotoxic agent for PC3 cells and to examine the role of acetyl-tubulin in docetaxel-resistant prostate cancer.

**Materials and Methods:** A series of docetaxel-resistant PC/DX cell subclones, were established by chronically exposing PC3 to progressively increased concentrations of docetaxel. Herein, we characterized the docetaxel-mediated cytotoxicity and molecular events in PC3 and PC/DX cells by MTT assay, Western blotting, RT-PCR, real-time PCR and flow cytometry analysis.

**Results:** Our results showed that levels of acetyl-tubulin,  $\alpha$ -tubulin,  $\beta$ -tubulin,  $\gamma$ -tubulin, and  $\beta$ III-tubulin were significantly higher expression in PC/DX25 than in parental PC3 cells by Western blotting analysis. PC/DX with greater resistance to docetaxel had higher levels of acetyl-tubulin and MCAK (mitotic centromere associate kinesin) than in PC3 cells. The expression of

acetyl-tubulin and MCAK was gradually increased by docetaxel in a dose- and time-dependent manner in PC3 cells. Histone deacetylase 6, a deacetyl enzyme of tubulin, mRNA and protein levels were significantly decreased in PC/DX25 than in PC3 cells. PC3 increased the chemoresistant ability to docetaxel by HDAC6 knockdown and Tubastain A (HDAC6 inhibitor), respectively. Conversely, PC/DX25 reversed the sensitivity to docetaxel by MCAK knockdown. Notably, MCAK knockdown in PC/DX25 induced cell cycle G2/M phase arrest after docetaxel treatment by flow cytometry analysis. Overexpression of Plk1 in PC3 increased the cell survival rate and resistance to docetaxel. Interestingly, we also found an evident up-regulation of acetyl-tubulin protein expression after recombinant epidermal growth factor treatment in a time-dependent manner in PC3 cells.

**Conclusion:** Up-regulation of acetyl-tubulin may play an important role in docetaxel-resistant prostate cancer.

#### IPD26:

#### SULF1 OVEREXPRESSION IS A POOR PROGNOSTIC FACTOR IN PATIENTS WITH UROTHELIAL CARCINOMA

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**Purpose:** Urothelial carcinoma (UC) originating from bladder (UBUC) and upper urinary tract (UTUC) is the most common tumor type of urinary tract. However, its pathogenesis remains obscured. Through data mining from a published transcriptomic database of UBUCs (GSE31684), we identified *SULF1* as the most significant gene showing upregulation from early tumor development to progression among those associated with growth factor activity (GO:0030201). Sulfatase-1 (*SULF1*), encoded by *SULF1*, is an extracellular 6-O-endosulfatase, which selectively removed 6-O-Sulfate from heparan sulfate proteoglycans (HSPGs), involving in multiple biologic processes including tumorigenesis and cancer progression proven in various cancers. However, the significance of *SULF1* expression has never been evaluated in UC. We therefore analyze its significance in our well-characterized cohort of UC.

**Materials and Methods:** Quantigene assay was used to detect *SULF1* messenger RNA (mRNA) level in 36 UTUCs and 30 UBUCs. Immunohistochemistry evaluated by H-score was used to determine *SULF1* protein expression in 296 UBUCs and 340 UTUCs. We then correlated protein expression status with clinicopathological features and evaluated the prognostic significance of *SULF1* protein expression for disease-specific survival (DSS) and metastasis-free survival (MeFS).

**Results:** Increments of *SULF1* transcript level were associated with higher pT status in both UTUC and UBUC (all  $P < 0.05$ ). *SULF1* protein overexpression was significantly associated with advanced primary tumor and nodal statuses, and presence of vascular invasion in both groups of UC. *SULF1* overexpression not only predicted worse DSS and MeFS by univariate analysis, but implied inferior DSS (UTUC,  $P < 0.001$ ; UBUC,  $P = 0.011$ ) and MeFS (UTUC,  $P < 0.001$ ; UBUC,  $P = 0.021$ ) in multivariate analysis.

**Conclusion:** *SULF1* overexpression is associated with advanced tumor status and implicated adverse clinical outcome for both patients of UTUC and UBUC. Our study unveiled the important role of *SULF1* expression in tumor progression in UC and may serve as a potential prognostic biomarker and a novel therapeutic target of UC.

#### IPD27:

#### CHEMOKINE CXCL14 (BRAK) EXPRESSION AND POTENTIAL ROLE IN HUMAN RENAL CELL CARCINOMA

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